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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/653,321	09/02/2003	Robert L. Lawton	BX/TF-101.P.1	3513

46251 7590 04/19/2007

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/653,321	LAWTON, ROBERT L.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,15-17,19-33,37-39 and 41-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15-17,19-33,37-39 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

AMENDMENT ENTRY

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/6/06 has been entered.

Following entry of Applicant's submission filed on 9/6/06, claims 1-11, 15-17, 19-33, 37-39 and 41-44 are pending and under examination.

OBJECTION(S)/REJECTION(S) OF RECORD WITHDRAWN

The amendment has overcome previously stated issues as follows:

All prior art rejection(s), for the following reasons:

Hendrickson et al teaches a DNA-antibody construct (i.e. a DNA-labeled antibody) that corresponds to the instantly recited "binding construct". When this construct is combined with a sample of analyte (corresponding to the instant "non-nucleic acid compound of interest"), a three-layer sandwich complex is formed on a solid phase (see Fig. 1). The DNA label (corresponding to the instant "nucleic acid portion") is then detected by PCR amplification. This detection is accomplished on the solid phase (see Fig. 1 and page 525 under "Immuno-PCR assay for single analytes"). There is no hint that one should detect the DNA-antibody construct that has not bound to analyte and that has thus remained in the solution phase of the reaction mixture obtained upon addition of the DNA-antibody construct (page 525, col. 1, last full para.). At best, this reference would be relevant for teachings of how one could make the instantly recited "binding construct" and how one could detect the PCR reaction products.

Ullman et al teaches an assay which uses a labeled binding partner (e.g. an antibody or antibody fragment). In the case in which the label is a polynucleotide

catalyst or an amplifiable polynucleotide sequence (col. 8, lines 16-31), the labeled binding partner would correspond to the instantly recited "binding construct". The "first reagent" of Ullman et al (e.g. col. 7, line 12-col. 10, line 3; col. 17, lines 7-45) is similar to the instantly recited "surfaces" (steps c) and d) of instant claim 1, steps d) and e) of instant claim 23), in that Ullman et al provides microparticles that have an analyte analog (corresponding to the instant "accessible non-nucleic acid binding targets"). The "first reagent" of Ullman et al, however, differs from the instant "surfaces" in that the "first reagent" of Ullman et al is not used to separate any of the other added reagents from a reaction mixture (no removing step is taught in Example 1). Rather, the "first reagent" of Ullman et al remains in the reaction mixture with the sample and other reagents and constitutes part of a signal-producing/detection system. The microparticles of the "first reagent" of Ullman et al thus have a purpose that is totally different from that of the "surfaces" used in the instant methods of claims 1 and 23. The microparticles of the "first reagent" of Ullman et al are manipulated in a totally different manner from that of the "surfaces" used in the instant methods of claims 1 and 23.

Piran et al teaches an assay which uses nothing corresponding to any reagent like the instantly recited "binding construct". The "insoluble material attached to an analyte derivative"/ "reagent 2" of Piran et al (e.g. col. 7, line 33-col. 8, line 39) is similar to the instantly recited "surfaces" (steps c) and d) of instant claim 1, steps d) and e) of instant claim 23), in that Piran et al provides liposomes that have an analyte analog (corresponding to the instant "accessible non-nucleic acid binding targets"). The "insoluble material attached to an analyte derivative"/ "reagent 2" of Piran et al is also similar to the instantly recited "surfaces" in that Piran et al uses this "reagent 2" to effectively remove excess antibody directed to an analyte, which is a "non-nucleic acid compound".

The assay format of Piran et al, however, differs from the instant format in that the fraction of antibody which has bound to/complexed with analyte/ "compound" is captured onto a solid phase ("Reagent 3") which bears a binder directed against the antibody, the label conjugated to the antibody, or the complex of antibody and analyte/

"compound". Piran et al teaches that the solid phase of "Reagent 3", with bound complexes attached thereto, is to be separated from other reaction components (col. 8, line 55). Piran et al teaches that bound complexes formed on this solid phase are then detected by a signal from the label (e.g. col. 8, lines 40-57). Piran et al thus directs one to detect a signal obtained from labeled antibody-antigen complexes that have been captured onto a solid phase, rather than (as instantly) detecting a signal from labeled antigen-antibody complexes that are in a solution phase (the examiner considers the instant "nucleic acid portion" as corresponding to a "label" as taught by Hendrickson et al, which teaches "DNA-labeled antibodies" and as taught by Ullman et al at col. 8, lines 15-31). Even in the case in which the solid phase of "Reagent 3", with bound complexes attached thereto, is not separated from other reaction components (col. 8, lines 56-57), the signal/label would still be detected from labeled antibody-antigen complexes that have been captured onto the solid phase, rather than from labeled antigen-antibody complexes that are in a solution phase.

Baez et al teaches the use of two nucleic acid-antibody constructs (i.e. DNA or RNA labeled antibodies) that corresponds to the instantly recited "binding construct". When these constructs are combined with a sample of analyte (corresponding to the instant "non-nucleic acid compound of interest") and with a capture reagent, a three-layer sandwich complex is formed on a solid phase, and the nucleic acid portions of each of the two nucleic acid-antibody constructs are able to interact to obtain a nucleic acid sequence that can be used to provide a detectable signal (see Figs 1 and 2). In this heterogeneous format (Figs. 1 and 2 and col. 12, lines 14-53), the detectable signal is obtained from labeled antibody-antigen complexes that have been captured onto the solid phase, rather than from labeled antigen-antibody complexes that are in a solution phase. In an alternative homogeneous format (col. 12, line 54-col. 13, line 18), in which the signal is obtained from antibody-antigen complexes that have been formed in solution, there is no use of any solid phase that would correspond to the instant "surfaces". Rather, the nucleic acid-antibody constructs that have not become bound to antigen are permitted to remain "free in solution" (col. 13, lines 4-8).

Since every one of the cited references of record that teaches a heterogeneous assay format teaches one to detect a label (Piran et al) or a nucleic acid (Hendrickson et al, Ullman et al, Baez et al) that is bound to a complex on a solid phase, there is nothing that would direct one to the instant invention by reading the references alone or by combining them. Also, since every one of the cited references of record that teaches one to use a homogenous assay format, that would detect a labeled complex in a solution phase (Piran et al or Baez et al), would not direct one to use any solid phase reagent corresponding to the instant "surfaces", there is nothing that would direct one to the instant invention by reading the references alone or by combining them.

Furthermore, the examiner finds little motivation to combine any of these references with each other for any aspect of their teachings. Only Hendrickson et al and Baez et al teach a DNA-antibody construct (i.e. a DNA-labeled antibody) that corresponds to the instantly recited "binding construct". Hendrickson et al uses this construct/conjugate in a three layer sandwich assay format, which is not like the assay format employed by Ullman et al, and which is not like the "type B" assay format of Piran et al. The sandwich assay format of Hendrickson et al, is like the "type A" assay format of Piran et al; however, in that case, the teachings of Piran et al would still lead one to detect labeled sandwich complexes that have been captured onto a solid phase, rather than to detect anything in a solution phase that would remain after removal of the solid phase therefrom. Likewise, Baez et al uses such a DNA-antibody construct/ conjugate in a three layer sandwich assay format, which is not like the assay format employed by Ullman et al, and which is not like the "type B" assay format of Piran et al. The sandwich assay format of Baez et al, is like the "type A" assay format of Piran et al; however, in that case, the teachings of Piran et al would still lead one to detect labeled sandwich complexes that have been captured onto a solid phase, rather than to detect anything in a solution phase that would remain after removal of the solid phase therefrom.

The claims are thus allowable over the prior art of record.

NEWLY STATED OBJECTION(S) TO CLAIMS

Claims 1, 23, 38 and 43 are objected to because of the following informalities:

In claim 1, part b), line 1 thereof, does applicant intend recitation of –or environmental— after "biological"?

In claim 23, part c), penultimate line thereof, does applicant intend recitation of –or environmental— after "biological"?

In claim 23, part e), line 4 thereof, it is believed applicant intends recitation of --targets— in lieu of "target".

In claim 38, does applicant intend dependency from claim 23, instead of 22?

In claim 43, line 2, does applicant intend recitation of –or environmental— after "biological"?

Appropriate correction is required.

NEWLY STATED REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 1-11, 15-17, 19-33, 37-39 and 41-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step f) "without the presence of any solid support" is unclear, since previous step e) has referred to "surfaces" rather than to "solid supports". Consistent terminology is required.

In claim 23, part e), penultimate line thereof, "said construct-complexes" lack antecedent basis. It is considered applicant intends to recite -- construct-compound complexes--.

In claim 23, in the preamble and in the "wherein" clause, "increased sensitivity" is unclear because one does not know what kind of detecting method has less sensitivity and thus serves as a baseline for comparison. Is the less sensitive, baseline method one that uses the same kinds of constructs and the same kind of detecting step(s), but one that does not have a separation step? Alternatively, is the less sensitive, baseline method one that uses the different kinds of constructs/reagents and/or detection step(s)?

Claims 6, 9, 28 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are:

With respect to the Markush group member recited as "detection of a label" one cannot determine what the "label" might be structurally connected to (e.g. is it a part of the "nucleic acid portion" of the "binding construct" or is it part of some other, unrecited reagent?) or how any "label" came to be present in the solution (e.g. has it been conjugated to the "binding construct" before step "mixing"/"contacting" step, or is it conjugated to some unrecited reagent that binds to the "nucleic acid portion" of the "binding construct"?).

With respect to the Markush group member recited as "enzymatic amplification" the recitation is incomplete, because one does not know what any enzyme is amplifying or how any enzyme is related to the components recited in the base claims. Is it amplification of the nucleic acid portion, or of some other component?

Further, the Markush group of claims 6, 9, 28 and 31 is improper because one cannot tell from the specification how the members have been disclosed such that they "possess at least one property in common which is mainly responsible for their function in the claimed relationship". See MPEP 2173.05(h). For example, since the processes of the "amplification" of a nucleic acid and the "detection of a label" would be distinct steps, one cannot determine how the recited Markush group members are properly considered to be alternatives of one another.

NEWLY STATED REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH

Claims 6, 9, 28 and 31 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The incorporation/attachment of the label to a nucleic acid hybridization probe is critical or essential to the practice of the invention, but such incorporation/attachment is not included in the claims. The claims

are thus not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

As noted supra under 112, second para., it is not clear how the Markush group member recited as "detection of a label" is to be conducted (e.g. one cannot determine what the "label" might be structurally connected to, or how any "label" came to be present in the solution). As far as the examiner can determine from the disclosure, the label is taught in the context of being incorporated in/attached to a nucleic acid hybridization probe (page 25). Since the examiner finds no other teaching of how a "label" is to be used in a detection method, the incorporation/attachment of the label to a nucleic acid hybridization probe is critical or essential to the practice of the invention.

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 4/10/07 DAS

David A Saunders

DAVID A. SAUNDERS
PRIMARY EXAMINER